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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference DC/BR70208	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR00/01728	International filing date (day/month/year) 21 June 2000 (21.06.00)	Priority date (day/month/year) 21 June 1999 (21.06.99)
International Patent Classification (IPC) or national classification and IPC C12Q 1/70		
Applicant BIO MERIEUX		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>6</u> sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>2</u> sheets.</p>	
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input checked="" type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>	

Date of submission of the demand 05 January 2001 (05.01.01)	Date of completion of this report 11 September 2001 (11.09.2001)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR00/01728

## I. Basis of the report

1. This report has been drawn on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

- ☒ the international application as originally filed.
- ☐ the description. pages 1-15 . as originally filed.  
 pages \_\_\_\_\_ . filed with the demand.  
 pages \_\_\_\_\_ . filed with the letter of \_\_\_\_\_  
 pages \_\_\_\_\_ . filed with the letter of \_\_\_\_\_
- ☐ the claims. Nos. 1-5 . as originally filed.  
 Nos. \_\_\_\_\_ . as amended under Article 19.  
 Nos. \_\_\_\_\_ . filed with the demand.  
 Nos. 6-14 . filed with the letter of 31/07/2001  
 Nos. \_\_\_\_\_ . filed with the letter of \_\_\_\_\_
- ☐ the drawings. sheets/fig \_\_\_\_\_ . as originally filed.  
 sheets/fig \_\_\_\_\_ . filed with the demand.  
 sheets/fig \_\_\_\_\_ . filed with the letter of \_\_\_\_\_  
 sheets/fig \_\_\_\_\_ . filed with the letter of \_\_\_\_\_

2. The amendments have resulted in the cancellation of:

- ☐ the description. pages \_\_\_\_\_
- ☐ the claims. Nos. \_\_\_\_\_
- ☐ the drawings. sheets/fig \_\_\_\_\_

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR 00/01728

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	1-14	YES
	Claims		NO
Inventive step (IS)	Claims	1-14	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-14	YES
	Claims		NO

## 2. Citations and explanations

## 1. The following documents are referred to:

- D1 WO-A-96/08580
- D2 Antimicrobial Agents and Chemotherapy, **42**(12), Dec. 1998, 3256-3265
- D3 Antimicrobial Agents and Chemotherapy, **40**(11), Nov. 1996, 2535-2541
- D4 Journal of Virology, **69**(9), Sept. 1995, 5431-5436
- D5 WO-A-90/14842
- D6 Journal of Biochemistry, **268**(15), June 1993, 11939-11945 (this document is cited by the applicant).

2. D1 describes a method for determining, in a biological sample taken from a patient contaminated with HIV 1, a possible resistance of the HIV 1 viral strain to treatment with an anti-protease agent, which involves searching for the presence of at least one position in the peptide sequence associated with resistance (D1, claims). D1 mentions two mutations which are particularly effective in inducing resistance: KN55N and L90M (D1, page 45, lines 16-19).

2.1 Similar methods are described in D2-D4:

D2 refers to the detection and identification of mutations in the peptide sequence of HIV 1 protease, which are associated with increased resistance to the anti-protease agent indinavir. The most significant mutations appear at positions 63, 84 and 90 and concern the ~~L63P~~, ~~I84V~~ and L90M substitutions (D2: abstract).

D3 describes a method for detecting mutations in HIV 1 protease associated with resistance to protease inhibitors. The method is applied to blood samples and the mutations concern positions 10, 46, 48, 63, 82, 84 and 90 (abstract and results).

D4 describes mutations at positions 48 and 90 of HIV 1 protease which increase resistance to the anti-protease agent Ro 31-8959 (abstract).

2.2 The methods defined in independent Claims 1 and 8 differ from the method known from D1-D4 in that the HIV 1 strain is replaced by HIV 2.  
The subject matter of independent Claims 1 and 8 is therefore novel (PCT Article 33(2)).

2.3 D5 describes a vaccine against HIV containing a modified protein of HIV 2. D5 discloses *inter alia* a nucleic acid sequence including the sequence CCA AGA ATA suitable for use in the method claimed in the present application (D5, page 7, line 4, and page 18, line 3). However, this sequence contains more than 40 nucleotides. Furthermore, none of the cited prior art documents describes the other samples defined in independent Claims 7 and 14. Consequently, the subject matter of these claims is also novel (PCT Article 33(2)).

3. The problem addressed by the present invention can therefore be considered to be that of providing a method and nucleotide samples for identifying mutations which render proteases of the HIV 2 strain resistant to anti-protease agents.

3.1 ~~At the time of~~ the invention, the amino acid sequence of the HIV 2 protease would have been known to a person skilled in the art (as indicated on page 2 of the application). He would also have been familiar with the fact that the sequences of the proteases of HIV 1 and HIV 2 are relatively conserved.

At first glance, it would therefore appear to be obvious for a person skilled in the art to follow the method of documents D1-D4 and, by virtue of the conservation between HIV 1 and HIV 2, to diagnose mutations in known positions, namely positions 10, 46, 48, 55, 63, 82, 84 and 90, thereby obtaining a method and nucleotide samples corresponding to Claims 1, 7, 8 and 14.

However, as illustrated by D6 (summary), it was also known that even apparently slight differences between the HIV 1 and HIV 2 strains could result in major differences. For instance, mutation of a single amino acid will not provide the predicted resistance but will increase sensitivity to a protease by a factor of 100.

3.2 In view of these facts, a person skilled in the art could not have anticipated the present invention as defined in independent Claims 1, 7, 8 and 14 and in dependent Claims 2-6 and 9-13.

The subject matter of Claims 1-14 is therefore inventive (PCT Article 33(3)).

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

Contrary to the requirements of PCT Rule 5.1(a)(ii), the description does not indicate the relevant prior art disclosed in D1-D5, nor does it cite these documents.

# PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For Receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) DC/BR70208

### Box No. I TITLE OF INVENTION

SEARCH METHOD FOR RESISTANCE TO ANTI-PROTEASES OF A STRAIN OF THE HIV-2 VIRUS FROM A BIOLOGICAL SAMPLE TAKEN FROM A PATIENT

### Box No. II APPLICANT

☐ This person is also inventor

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

BIO MERIEUX  
69280 MARCY - L'ETOILE - FRANCE

Telephone No.

Facsimile No.

Teleprinter No.

Applicant's registration No. with the Office

State (that is, country) of nationality:

FRANCE

State (that is, country) of residence:

FRANCE

This person is applicant for the purposes of:

☐

all designated States

☒

all designated States except the United States of America

☐

the United States of America only

☐

the States indicated in the Supplemental Box

### Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS  
3 Avenue Victoria  
75004 PARIS - FRANCE

This person is:

☒

applicant only

☐

applicant and inventor

☐

inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

FRANCE

State (that is, country) of residence:

FRANCE

This person is applicant for the purposes of:

☐

all designated States

☒

all designated States except the United States of America

☐

the United States of America only

☐

the States indicated in the Supplemental Box

☒

Further applicants and/or (further) inventors are indicated on a continuation sheet.

### Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒

agent

☐

common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

TONNELIER Jean-Claude  
NONY & ASSOCIATES  
29, Rue Cambacérès  
75008 PARIS  
FRANCE

Telephone No.  
01 43 12 84 60

Facsimile No.  
01 43 12 84 70

Teleprinter No.

Agent's registration No. with the Office

☐

Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

**Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)**

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

TELLES Jean-Noël  
33, Rue Dautancourt  
75017 PARIS - FRANCE

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

FRANCE

State (that is, country) of residence:

FRANCE

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☒

the United States of America only

☐

the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

BRUN-VEZINET Françoise  
24 Boulevard St Germain  
75005 PARIS - FRANCE

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

FRANCE

State (that is, country) of residence:

FRANCE

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☒

the United States of America only

☐

the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

DESCAMPS Diane  
85 Boulevard Pasteur  
75015 PARIS - FRANCE

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

FRANCE

State (that is, country) of residence:

FRANCE

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☒

the United States of America only

☐

the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☐

the United States of America only

☐

the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.



**Box No. V DESIGNATION OF STATES**

Mark the applicable check-boxes below; at least one must be marked.

The following designations are hereby made under Rule 4.9(a): **(Double-click here if you want all the boxes below checked.)****Regional Patent**

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH & LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, TR Turkey, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)*.....

**National Patent** *(if other kind of protection or treatment desired, specify on dotted line):*

- |  |   |   |
|--|---|---|
| <input checked="" type="checkbox"/> <b>AE</b> United Arab Emirates                   | <input checked="" type="checkbox"/> <b>GE</b> Georgia .....             | <input checked="" type="checkbox"/> <b>MW</b> Malawi .....                      |
| <input checked="" type="checkbox"/> <b>AG</b> Antigua and Barbuda                    | <input checked="" type="checkbox"/> <b>GH</b> Ghana .....               | <input checked="" type="checkbox"/> <b>MX</b> Mexico .....                      |
| <input checked="" type="checkbox"/> <b>AL</b> Albania .....                          | <input checked="" type="checkbox"/> <b>GM</b> Gambia .....              | <input checked="" type="checkbox"/> <b>MZ</b> Mozambique .....                  |
| <input checked="" type="checkbox"/> <b>AM</b> Armenia .....                          | <input checked="" type="checkbox"/> <b>HR</b> Croatia .....             | <input checked="" type="checkbox"/> <b>NO</b> Norway .....                      |
| <input checked="" type="checkbox"/> <b>AT</b> Austria .....                          | <input checked="" type="checkbox"/> <b>HU</b> Hungary .....             | <input checked="" type="checkbox"/> <b>NZ</b> New Zealand .....                 |
| <input checked="" type="checkbox"/> <b>AU</b> Australia .....                        | <input checked="" type="checkbox"/> <b>ID</b> Indonesia .....           | <input checked="" type="checkbox"/> <b>PL</b> Poland .....                      |
| <input checked="" type="checkbox"/> <b>AZ</b> Azerbaijan .....                       | <input checked="" type="checkbox"/> <b>IL</b> Israel .....              | <input checked="" type="checkbox"/> <b>PT</b> Portugal .....                    |
| <input checked="" type="checkbox"/> <b>BA</b> Bosnia and Herzegovina .....           | <input checked="" type="checkbox"/> <b>IN</b> India .....               | <input checked="" type="checkbox"/> <b>RO</b> Romania .....                     |
|  | <input checked="" type="checkbox"/> <b>IS</b> Iceland .....             | <input checked="" type="checkbox"/> <b>RU</b> Russian Federation .....          |
| <input checked="" type="checkbox"/> <b>BB</b> Barbados .....                         | <input checked="" type="checkbox"/> <b>JP</b> Japan .....               |   |
| <input checked="" type="checkbox"/> <b>BG</b> Bulgaria .....                         | <input checked="" type="checkbox"/> <b>KE</b> Kenya .....               | <input checked="" type="checkbox"/> <b>SD</b> Sudan .....                       |
| <input checked="" type="checkbox"/> <b>BR</b> Brazil .....                           | <input checked="" type="checkbox"/> <b>KG</b> Kyrgyzstan .....          | <input checked="" type="checkbox"/> <b>SE</b> Sweden .....                      |
| <input checked="" type="checkbox"/> <b>BY</b> Belarus .....                          | <input checked="" type="checkbox"/> <b>KP</b> Democratic People's ..... | <input checked="" type="checkbox"/> <b>SG</b> Singapore .....                   |
| <input checked="" type="checkbox"/> <b>BZ</b> Belize .....                           | Republic of Korea .....   | <input checked="" type="checkbox"/> <b>SI</b> Slovenia .....                    |
| <input checked="" type="checkbox"/> <b>CA</b> Canada .....                           | <input checked="" type="checkbox"/> <b>KR</b> Republic of Korea .....   | <input checked="" type="checkbox"/> <b>SK</b> Slovakia .....                    |
| <input checked="" type="checkbox"/> <b>CH &amp; LI</b> Switzerland and Liechtenstein | <input checked="" type="checkbox"/> <b>KZ</b> Kazakhstan .....          | <input checked="" type="checkbox"/> <b>SL</b> Sierra Leone .....                |
| <input checked="" type="checkbox"/> <b>CN</b> China .....                            | <input checked="" type="checkbox"/> <b>LC</b> Saint Lucia .....         | <input checked="" type="checkbox"/> <b>TJ</b> Tajikistan .....                  |
| <input checked="" type="checkbox"/> <b>CO</b> Colombia .....                         | <input checked="" type="checkbox"/> <b>LK</b> Sri Lanka .....           | <input checked="" type="checkbox"/> <b>TM</b> Turkmenistan .....                |
| <input checked="" type="checkbox"/> <b>CR</b> Costa Rica .....                       | <input checked="" type="checkbox"/> <b>LR</b> Liberia .....             | <input checked="" type="checkbox"/> <b>TR</b> Turkey .....                      |
| <input checked="" type="checkbox"/> <b>CU</b> Cuba .....                             | <input checked="" type="checkbox"/> <b>LS</b> Lesotho .....             | <input checked="" type="checkbox"/> <b>TT</b> Trinidad and Tobago .....         |
| <input checked="" type="checkbox"/> <b>CZ</b> Czech Republic .....                   | <input checked="" type="checkbox"/> <b>LT</b> Lithuania .....           |   |
| <input checked="" type="checkbox"/> <b>DE</b> Germany .....                          | <input checked="" type="checkbox"/> <b>LU</b> Luxembourg .....          | <input checked="" type="checkbox"/> <b>TZ</b> United Republic of Tanzania ..... |
| <input checked="" type="checkbox"/> <b>DK</b> Denmark .....                          | <input checked="" type="checkbox"/> <b>LV</b> Latvia .....              | <input checked="" type="checkbox"/> <b>UA</b> Ukraine .....                     |
| <input checked="" type="checkbox"/> <b>DM</b> Dominica .....                         | <input checked="" type="checkbox"/> <b>MA</b> Morocco .....             | <input checked="" type="checkbox"/> <b>UG</b> Uganda .....                      |
| <input checked="" type="checkbox"/> <b>DZ</b> Algeria .....                          | <input checked="" type="checkbox"/> <b>MD</b> Republic of Moldova ..... | <input checked="" type="checkbox"/> <b>US</b> United States of America ..       |
| <input checked="" type="checkbox"/> <b>EE</b> Estonia .....                          |   |   |
| <input checked="" type="checkbox"/> <b>ES</b> Spain .....                            | <input checked="" type="checkbox"/> <b>MG</b> Madagascar .....          | <input checked="" type="checkbox"/> <b>UZ</b> Uzbekistan .....                  |
| <input checked="" type="checkbox"/> <b>FI</b> Finland .....                          | <input checked="" type="checkbox"/> <b>MK</b> The former Yugoslav ..... | <input checked="" type="checkbox"/> <b>VN</b> Viet Nam .....                    |
| <input checked="" type="checkbox"/> <b>GB</b> United Kingdom .....                   | Republic of Macedonia .....   | <input checked="" type="checkbox"/> <b>YU</b> Yugoslavia .....                  |
| <input checked="" type="checkbox"/> <b>GD</b> Grenada .....                          |   | <input checked="" type="checkbox"/> <b>ZA</b> South Africa .....                |
|  | <input checked="" type="checkbox"/> <b>MN</b> Mongolia .....            | <input checked="" type="checkbox"/> <b>ZW</b> Zimbabwe .....                    |

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet

<input type="checkbox"/> .....	<input type="checkbox"/> .....	<input type="checkbox"/> .....
<input type="checkbox"/> .....	<input type="checkbox"/> .....	<input type="checkbox"/> .....

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except the designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

**Box No. VI PRIORITY CLAIM**

The priority of the following earlier application(s) is hereby claimed:

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1) 21 June 1999	99 07855	FRANCE		
item (2)				
item (3)				
item (4)				
item (5)				

☐ Further priority claims are indicated in the Supplemental Box.

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of this international application is the receiving Office) identified above as:

☐ all items   
 ☐ item (1)   
 ☐ item (2)   
 ☐ item (3)   
 ☐ item (4)   
 ☐ item (5)   
 ☐ other, see Supplemental Box

\*Where the earlier application is an ARIPO application, indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed (Rule 4.10(b)(ii)): .....

**Box No. VII INTERNATIONAL SEARCHING AUTHORITY**

**Choice of International Searching Authority (ISA)** (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / .....

**Request to use results of earlier search: reference to that search** (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)	Number	Country (or regional Office)
10 May 2000	FA 576397	OEB

**Box No. VIII DECLARATIONS**

The following declarations are contained in Boxes Nos. VIII (i) to (v) (mark the applicable check-boxes below and indicate in the right column the number of each type of declaration):

		Number of declarations
<input type="checkbox"/> Box No. VIII (i)	Declaration as to the identity of the inventor	:
<input type="checkbox"/> Box No. VIII (ii)	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	:
<input type="checkbox"/> Box No. VIII (iii)	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	:
<input type="checkbox"/> Box No. VIII (iv)	Declaration of inventorship (only for the purposes of the designation of the United States of America)	:
<input type="checkbox"/> Box No. VIII (v)	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty:	:

**Box No. IX CHECK LIST; LANGUAGE OF FILING**

This international application contains:

(a) the following number of sheets in paper form:

request (including declaration sheets)

4

description (excluding sequence listing part)

: 15

claims

: 3

abstract

: 1

drawings

: \_\_\_\_\_

**Sub-total number of sheets** :sequence listing part of description (*actual number of sheets if filed in paper form, whether or not also filed in computer readable form; see (b) below*)

: \_\_\_\_\_

**Total number of sheets** : 23

(b) sequence listing part of description filed in computer readable form

(i) ☐ only (under Section 801(a)(i))(ii) ☐ in addition to being filed in paper form (under Section 801(a)(ii))**Type and number of carriers** (diskette, CD-ROM, CD-R or other) on which the sequence listing part is contained (*additional copies to be indicated under item 9(ii), in right column*):This international application is **accompanied by** the following item(s) (mark the applicable check-boxes below and indicate in right column the number of each item):

Number of items

1. ☐ fee calculation sheet :
2. ☐ original separate power of attorney :
3. ☐ original general power of attorney :
4. ☐ copy of general power of attorney; reference number, if any: \_\_\_\_\_ :
5. ☐ statement explaining lack of signature :
6. ☐ priority document(s) identified in Box No. VI as item(s): \_\_\_\_\_ :
7. ☐ translation of international application into (language): \_\_\_\_\_ :
8. ☐ separate indications concerning deposited microorganism or other biological material :
9. ☐ sequence listing in computer readable form (indicate also type and number of carriers (diskette, CD-ROM, CD-R or other ))
  - (i) ☐ copy submitted for the purposes of international search under Rule 13ter only (and not as part of the international application) :
  - (ii) ☐ (*only where check-box (b)(i) or (b)(ii) is marked in left column*) additional copies including, where applicable, the copy for the purposes of international search under Rule 13ter :
  - (iii) ☐ together with relevant statement as to the identity of the copy or copies with the sequence listing part mentioned in left column :
10. ☒ other (*specify*) Search Report \_\_\_\_\_ :

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Paris, 21 June 2000

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